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14. ABSTRACT
Introduction. Over 80% altitude decompression sickness (DCS) was reported during a 4-h exposure with mild exercise to 7620 m (25,000 ft) without prebreathe. Prebreathe for more than 1 h would be necessary to reduce the DCS risk below 40%. Use of a single period of exercise to enhance prebreathe effectiveness has been successfully tested and used during some U-2 operations. The current tests used multiple exercise sessions to enhance prebreathe (MEEP) as a means of improving denitrogenation efficiency. Methods. Two MEEP profiles, 30 or 60 min, preceded 4-h exposures to 7620 m with mild, upper-body exercise while breathing 100% oxygen. Resting prebreathe controls were from published studies at the same laboratory. Both MEEP profiles involved 10 min of strenuous dual-cycle ergometry (75% of maximal oxygen uptake) at the beginning of prebreathe. After a 15-min rest period during the 60-min prebreathe an additional 5 min of strenuous ergometry was performed. Mild exercise was performed during 15 of the last 20 min of both prebreathe profiles. Results. The 60-min MEEP resulted in 25% DCS and the 30-min MEEP 40% DCS (N.S.). The 25% incidence of DCS following the 60-min MEEP profile was significantly less than the 63% DCS following an equal-time, resting prebreathe control. Following the 30-min MEEP, DCS incidence was not greater than the incidence following a 60-min, resting prebreathe control. There was a lower incidence of venous gas emboli during the MEEP exposures than during resting control exposures. Conclusion. Denitrogenation with multiple periods of exercise provides a shorter alternative to resting prebreathe for reducing DCS risk during exposure to 7620 m.

15. SUBJECT TERMS
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RESEARCH ARTICLE

Altitude Decompression Sickness at 7620 m Following Prebreathe Enhanced with Exercise Periods

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Webb JT, Pilmanis AA, Balldin UI, Fischer JR Jr. Altitude decompression sickness at 7,620 m following prebreathe enhanced with exercise periods. Aviat Space Environ Med 2004;75:

Introduction. Over 80% altitude decompression sickness (DCS) was reported during a 4-h exposure with mild exercise to 7620 m (25,000 ft) without prebreathe. Prebreathe for more than 1 h would be necessary to reduce the DCS risk below 40%. Use of a single period of exercise to enhance prebreathe effectiveness has been successfully tested and used during some U-2 operations. The current tests used multiple exercise sessions to enhance prebreathe (MEEP) as a means of improving denitrogenation efficiency. **Methods.** Two MEEP profiles, 30 or 60 min, preceded 4-h exposures to 7620 m with mild, upper-body exercise while breathing 100% oxygen. Resting prebreathe controls were from published studies at the same laboratory. Both MEEP profiles involved 10 min of strenuous dual-cycle ergometry (75% of maximal oxygen uptake) at the beginning of prebreathe. After a 15-min rest period during the 60-min prebreathe an additional 5 min of strenuous ergometry was performed. Mild exercise was performed during 15 of the last 20 min of both prebreathe profiles. **Results.** The 60-min MEEP resulted in 25% DCS and the 30-min MEEP 40% DCS (N.S.). The 25% incidence of DCS following the 60-min MEEP profile was significantly less than the 63% DCS following an equal-time, resting prebreathe control. Following the 30-min MEEP, DCS incidence was not greater than the incidence following a 60-min, resting prebreathe control. There was a lower incidence of venous gas emboli during the MEEP exposures than during resting control exposures. **Conclusion.** Denitrogenation with multiple periods of exercise provides a shorter alternative to resting prebreathe for reducing DCS risk during exposure to 7620 m.

Keywords: DCS; hypobaric; preoxygenation; venous gas emboli

Some unpressurized, military aircraft are capable of extended cruise at 7620 m (25,000 ft) or higher. Decompression sickness (DCS) risk during such high altitude exposures can be reduced by breathing 100% oxygen before exposure (prebreathing) to lower the nitrogen content in the tissues and blood of those exposed. The use of prebreathing complicates preparation for operational missions due to its time requirements. However, during 4 or more h of exposure to 7620 m without the use of prebreathing, DCS incidence can be higher than 80% (14). Such levels of DCS symptoms are generally considered unacceptable for normal flying operations (2,13). Minimizing prebreathe time while reducing DCS risk to an acceptable level is an attractive objective.

A study at the Air Force Research Laboratory (AFRL), Brooks City-Base, TX, involving a 1-h, resting prebreathe prior to 4-h exposures to 7620 m yielded 63% DCS (15). To reduce that level of DCS to a more operationally acceptable level, below 40%, it follows that more denitrogenation (longer prebreathe) would be needed (18). A 40% DCS incidence is half of the zero-prebreathe incidence (7,16).

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Exercise-enhanced prebreathe (EEP) increases denitrogenation efficiency. It can reduce the prebreathe time required to achieve a given level of protection compared with a resting prebreathe. Alternatively, without changing total prebreathe time, including EEP would lower the level of risk (1,13).

The use of upper and lower-body exercise for 10 min at 75% of VO_{2peak} while breathing 100% oxygen is sufficient to greatly increase perfusion, ventilation, and diffusion while insufficient to induce fatigue. The increased perfusion, ventilation, and diffusion is thought to create a steep concentration gradient for nitrogen to follow from the tissues to the capillaries, where it is carried to the lungs for expiration (13,16). A single-exercise-enhanced prebreathe (single-EEP) method was tested and used during some U-2 high altitude reconnaissance operations (5). During the operational testing of this procedure (5), a pilot used several exercise methods involving upper and lower-body sub-maximal exercise. Using EEP, this pilot, previously grounded for high susceptibility to DCS during high altitude flights, was able to continue and complete his career in high-flying aircraft.

Multiple-exercise-enhanced prebreathe (MEEP) may further reduce DCS risk. A NASA-sponsored multi-center trial using a MEEP of 2 h was successful in reducing DCS incidence relative to a single-EEP of the same duration (4). Their result allowed a time-saving modification to denitrogenation procedures prior to extravehicular activity (EVA) from the International Space Station to an equivalent pressure altitude of 9144 m during EVA.

TABLE I. SUBJECT ANTHROPOMETRY

Profile	N	Wt, kg	Ht, m	BMI	Body Fat, %	Age
60-min MEEP	40	83.6	1.77	26.4	16.2*	32.9
30-min MEEP	40	83.5	1.77	26.6	16.3†	32.0

BMI = $Wt \cdot Ht^{-2}$
MEEP = Multiple, exercise-enhanced prebreathe
* N=37
† N=38

The results of that NASA study (4) indicated that MEEP may reduce DCS incidence to a level commensurate with operational planning for exposures to 7620 m in unpressurized USAF aircraft and prompted the use of a modified MEEP procedure during the current study. The purpose of this study was to test 60 and 30-min MEEP procedures. A 60-min resting prebreathe is well established as a standard for USAF operational use during exposures to altitudes (cabin pressures) above 7620 m. A 30-min MEEP profile at 7620 m was added because it would be more operationally acceptable.

METHODS

Human subjects, 42 men and 10 women, participated in 80 altitude chamber exposures. There were 4 women and 24 men who completed both prebreathe profiles. There were an additional 3 women and 9 men who completed one exposure each of the 2 profiles for a total of 33 men and 7 women in each profile. The equal number of men and women in each profile allowed averaging of anthropometrics for the entire set of subjects who accomplished each prebreathe scenario (Table I).

The non-smoking (for preceding 2 years), military or contract-acquired subjects were between the ages of 18-45. The voluntary, fully-informed consent of the subjects used in this research was obtained in accordance with AFI 40-402. The Brooks Institutional Review Board and the USAF Surgeon General's Research Oversight Committee approved the protocol. All subjects passed an appropriate physical examination, and were representative of the USAF rated aircrew population in terms of age, height, weight, and fitness (Table I). Female subjects had a negative pregnancy test within 36 hours prior to each altitude exposure.

Subjects were trained on the use of oxygen equipment and safety procedures before any research exposures. Subjects were not queried as to their health or well-being during the altitude exposure. However, they received a briefing on the morning of the exposure which emphasized their responsibility to inform the chamber personnel of any such changes.

The altitude exposures were conducted in an AFRL hypobaric research chamber at Brooks City-Base, TX. An aerospace physiologist was on call in the chamber vicinity for all subject exposures. Trained personnel assisted with and maintained all oxygen and communications equipment, monitored the chamber pressure and oxygen concentration, and watched for adverse subject reactions. A listing of possible DCS symptoms was posted on the inside wall of the chamber, where it could be viewed during the test by subjects who were instructed to monitor their own condition. All of the chamber personnel, including the research technicians, investigators, and medical observers were trained to recognize DCS signs and symptoms in subjects. The subjects were also trained to recognize DCS symptoms, how to report their occurrence and progress, and were encouraged to do so expeditiously. If chamber personnel felt the subject was experiencing unrecognized or serious DCS symptoms, they could initiate recompression and additional interventions in coordination with the physiologist or local dive medicine experts, as necessary. Hyperbaric medicine personnel and facilities were immediately available on site to treat DCS that persisted at ground level.

Before the experiment started, subjects accomplished a communication and ear and sinus pressure equalization check while the altitude chamber was decompressed to provide a simulated altitude of 1524 m (5000 ft) and recompressed to ground level at a rate of 1524 $m \cdot min^{-1}$. Time spent at the simulated 1524-m was altitude less than 5 sec. The rate of pressure change was 1524 m/min. The subjects donned an Intertechnique neck seal respirator and breathed 100% oxygen during prebreathe, ascent, exposure, descent, and post-breathing. It provided a slight, 2 cm of water, positive pressure which reduced the opportunity for inboard leaks of nitrogen from ambient air. An aviator-type mask was used during some post-breathing.

AFRL medical observers ensured subject health and safety, and made the diagnosis of DCS. These medical observers were not investigators on the protocol, which ensured an unbiased diagnosis. Subjects were alone in the chamber while at simulated altitude during those exposures accomplished after installation of a robotic arm assembly used to manipulate the echo-imaging probe (10). Subjects were accompanied by an inside observer who operated the probe prior to installation of the robotic arm. The subjects were instructed to report any changes to the medical observer and the determination to terminate the exposure was made from these reports. The subject was examined after recompression to ground level. The medical observers were trained in the diagnosis of DCS and had the ability to consult with the physicians in Hyperbaric Medicine. Endpoints of the exposures were 1) completion of the scheduled exposure time; 2) diagnosis of DCS signs and/or symptoms; 3) evidence of left ventricular gas emboli. The altitude DCS endpoint criteria are fully described in Pilmanis et al. (10). These criteria were posted at the chamber and used by the medical observers in conjunction with good medical judgment for the DCS diagnosis.

Subjects with symptoms requiring potential additional care were referred to the on-site Hyperbaric Medicine staff where they were evaluated and treated with hyperbaric oxygen therapy as necessary. After the exposures, the subjects were given a written list of possible signs and symptoms of DCS. They were told to contact the Hyperbaric Medicine staff in the event of recurring or delayed problems resulting from their hypobaric exposure.

Precordial echo imaging for venous gas emboli (VGE) was nominally accomplished four times per hour using a Hewlett-Packard® SONOS 1000 Echo Imaging System (Andover, Massachusetts) as fully described in Pilmanis et al. (10). VGE were graded by the method of Spencer (11).

Exposure profiles consisted of a 4-h exposure to 7620 m while accomplishing mild, upper-body exercises identical to those performed during previous studies (2,13,14,16). The prebreathe scenarios were designed to be compatible with time constraints implied by operational activities and utilized a dual-cycle ergometer as the exercising mode. $\dot{V}O_{2max}$ was estimated from results of US Air Force submaximal

cycle ergometry tests completed earlier. That testing used a computerized speed and resistance algorithm resulting in an estimated $\dot{V}O_{2max}$ (6). The subjects average $\dot{V}O_{2max}$ was 3.1 $L \cdot min^{-1}$. Subjects' $\dot{V}O_{2max}$ was used to calculate individualized workload during the prebreathe exercise. The leg ergometry constituted 80% of the total work (16).

TABLE II. RESULTS OF EXPOSURES TO 7620 M FOR 4 H WITH MILD EXERCISE

Prebreathe	N	VGE	Grade 4 VGE	DCS
60-min MEEP	40	55%[§**]	25%[§**]	25%[§**]
30-min MEEP	40	65%[§**]	45%	43%[**]
60-min Rest[*]	27	85%	56%	63%
30-min Rest[†]	31	90%	68%	61%
Zero[‡]	35	86%	53%	80%

[*] (15)
[†] (8) This profile used mild cycle ergometry.
[‡] (14)
[§] Significantly ($P < 0.05$) less incidence than during equal-time resting prebreathe control.
[**] Significantly ($P < 0.05$) less incidence than during zero prebreathe control.

60-min multiple-exercise-enhanced prebreathe (60-min MEEP)

The 60-min MEEP consisted of a 2-min warm up; 8 min dual-cycle ergometry at 75% $\dot{V}O_{2max}$; 15-min rest; 2-min warm up; 3 min dual-cycle ergometry at 75% $\dot{V}O_{2max}$; 10-min rest; 15-min dual-cycle ergometry at 30% $\dot{V}O_{2max}$; 5-min transition to the chamber.

30-min multiple-exercise-enhanced prebreathe (30-min MEEP)

The 30-min MEEP consisted of a 2-min warm up; 8 min dual-cycle ergometry at 75% $\dot{V}O_{2max}$; 15-min dual-cycle ergometry at 30% $\dot{V}O_{2max}$; 5-min transition to the chamber.

Controls for the two tests were from Pilmanis et al. (8) and (15) as shown in Table II. They involved resting prebreathe with 100% oxygen prior to exposures to 7620 m with mild exercise. An exposure scenario using zero prebreathe was also included in Table II to show the high, 80% incidence of DCS at that altitude (14).

Chi Square tests were used to determine if differences existed between results from the two MEEP prebreathe scenarios or between the test exposure results and controls. McNemar's test was used to determine if a difference existed between the subjects' responses for the subset of 4 females and 24 males who accomplished both scenarios.

RESULTS

Fig. 1 and Table II show results of the 60-min MEEP and 30-min MEEP. The 25% DCS observed at 7620 m after the 60-min MEEP is significantly less than the reported 80% incidence observed without prebreathe or the 63% incidence with a 60-min resting prebreathe ($P<0.01$). It is also commensurate with incidence following the recommended resting prebreathe scenarios prior to EVA from the Space Shuttle (12). The 30-min MEEP result of 43% DCS was lower than the 81% DCS without prebreathe ($P < 0.001$).

The coincidence of both Grade 4 VGE and DCS being 25% following the 60-min MEEP does not indicate correspondence between Grade 4 VGE and DCS. Of the 10 subjects with symptoms, only 5 developed Grade 4 VGE and 5 that developed Grade 4 VGE did not develop DCS. A similar relationship following the 30-min MEEP agrees with previous findings that show high grades of VGE are inadequate predictors of DCS (2), being no more effective than coin flipping. Indeed, the data on Grade 4 VGE and DCS from those experiments (2) shows nearly twice as many exposures (n=26) in which the two were not synonymous vs exposures in which they corresponded (n=14) in the combined test and control exposures.

Despite the lack of correlation between Grade 4 VGE and DCS in specific individuals, there is a well-established relationship between VGE or Grade 4 VGE and level of exposure severity. Therefore the data are consistent and mutually supporting, if not predictive.

Comparison between the two MEEP tests' levels of DCS, Gr4 VGE, or VGE showed no significant differences ($P>0.05$). The 28 subjects who accomplished both profiles showed no significant difference between their DCS or VGE responses ($P>0.15$). The 30-min MEEP did result in more Grade 4 VGE than the 60-min MEEP in the intra-subject comparison (McNemar's Test; $P < 0.05$).

DISCUSSION

The 60-min MEEP procedure VGE, Grade 4 VGE, and DCS incidences were significantly less than following resting, equal-time prebreathe controls ($P < 0.03$; Table II) or following no prebreathe ($P < 0.02$). This result met the goal of significantly reducing the incidence of DCS or the prebreathe time relative to resting prebreathe. The potential for substantial reduction in symptom development is apparent if the procedure were to be implemented. The 30-min MEEP resulted in less VGE than the 30-min resting prebreathe control ($P < 0.05$; Table II). It also showed a trend ($P < .08$) toward less Grade 4 VGE than the 30-min resting prebreathe control. The 30-min MEEP resulted in 21% less DCS, but this was not significantly different ($P = 0.10$) from the DCS incidence following the longer, 60-min resting prebreathe control.

The success of MEEP during NASA trials is accepted (4) and provides validation of the MEEP concept. However, a direct comparison of a short MEEP with an equal-duration single-EEP could be useful in designing better operational procedures to include simulation of activity involved in operational prebreathe.

Mild exercise

The AFRL DCS Research Database contains data on many exposures at or near 9144 m which could be used as controls for evaluating the effects of exercise enhancement of prebreathe. The mild exercises involved in one experiment at 9144 m (15) yielding 87% DCS may have had more influence on eliciting DCS than the mild exercises performed during the current study. That 87% DCS was observed during performance of mild upper <u>and</u> lower-body exercise during 4-h, 9144-m exposures following a 1-h resting prebreathe (15). It is higher than the level reported at 9144 m elsewhere in the literature from Brooks (9,13,17). The slightly lower altitude used in two of these studies with lower DCS could not account for such differences (Table III). The major difference in the exposure conditions was the type of exercise performed at altitude.

Comparison between the effects of mild exercise involving the upper <u>and</u> lower-body with mild exercise of only the upper-body may provide some clarification. Indeed, mild exercise may be a broader term than the 8-20% of $\dot{V}O_{2max}$ exercise cycle average indicates. The variation in exercise intensity as judged by the % of $\dot{V}O_{2max}$ or even the duration of rest periods may not adequately explain the differences. The relatively high intensity of stress on the lower joints during chair-height knee bend exercises may provide a better explanation of the 87% DCS described by Webb and Pilmanis (15). The various DCS incidences in Table III may show why it is better to use a study with a very closely-matched exercise as a control to ensure similarity of exposure severity. However, with the best control for EEP exposures at 9144 m being a resting prebreathe followed by mild, upper-body exercise during exposure, the N is limited to 28 (13). That profile's DCS incidence of 75% is 10% greater than the 65% DCS incidence of all 137 exposures summarized in Table III.

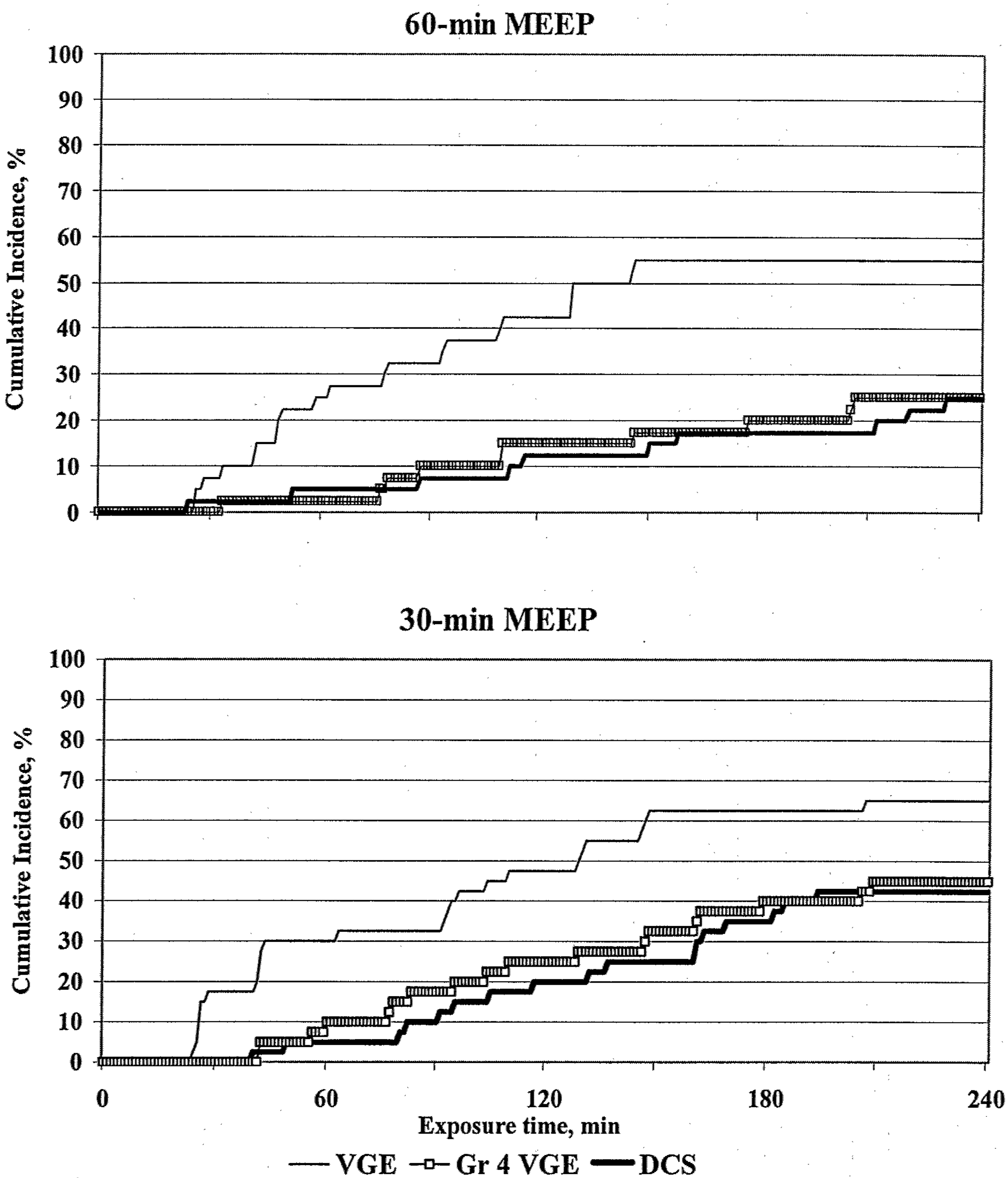

Fig. 1. Cumulative Onset of VGE and DCS during the 60-min MEEP and 30-min MEEP.

Comparison of EEP with resting prebreathe

Review of several, very similar EEP experiments and their controls could help verify the validity of EEP as a viable procedure to reduce DCS risk. Including all Brooks City-Base experimental EEP results and their controls, regardless of the specific exercise schedule utilized during prebreathe, enables more powerful statistical analyses. With additional statistical evidence regarding the effectiveness of EEP, better decisions could be made regarding experimentation to further clarify any advantage of MEEP.

TABLE III. RESULTS OF 4-H, 8992 TO 9144-M EXPOSURES FOLLOWING A 1-H, RESTING PREBREATHE.

Study Reference	N	% of VO_{2max}	Type Exercise	% DCS
(15)*	30	15-20**	Upper & Lower Body	87
(13)†	28	15-20	Upper Body	75
(17)‡	38	10-12	Upper Body	61
(9)§	41	8-10	Upper or Lower Body	59
Sum/Mean	137	--	-	65

Note: Only a subject's first exposure under any specific condition was used.
* Exposures to 9144 m with five chair-height knee bend exercises and 5# dumbbell lifts with each arm every 15 min
† Exposures to 9144 m with 3 exercise stations, 12 of every 16 min
‡ Exposures to 8992 m with 1 exercise station, 5 of every 15 min
§ Exposures to 8992 m with 1 exercise station, 4 of every 20 min

To evaluate the effectiveness of EEP, we took data from Table II and all previous EEP research at Brooks City-Base (2,8,13,15,16). EEP (single and MEEP) and resting prebreathe controls for those exposures are reviewed in Table IV. These data used the same facilities, associated procedures and investigators. All but the current two studies and their controls (Table II) involved exposure to 9,144 m. By combining the results from more than one altitude, the resulting DCS incidences in Table IV are not indicative of results at a specific altitude. However, with the appropriate controls at each altitude, the relative incidence with and without the benefit of EEP should be discernable (Fig. 2). The results in Table IV indicate exercise-enhanced prebreathe is more effective than resting prebreathe in preventing DCS ($P < 0.0001$). The increased perfusion, ventilation, and diffusion while breathing 100% oxygen leads to delivery of nitrogen-free blood to the tissues during the exercise and remaining prebreathe. This is believed to set up a steep gradient within the tissues. The increased gradient apparently results in much faster clearance of nitrogen by the lungs than during resting prebreathe.

TABLE IV. RESULTS OF RESTING VS. EXERCISE-ENHANCED PREBREATHE PRIOR TO 4-H EXPOSURE WITH MILD EXERCISE - 9144 m and 7620 m

Prebreathe	VGE	Grade 4 VGE	DCS
Resting, N*	261	261	261
Incidence	**77%**	**48%**	**65%**
Mean latency, min	80	98	102
Exercise-Enhanced, N†	219	219	219
Incidence	**64%**	**31%**	**42%**
Mean latency, min	80	117	108
Incidence, P <	**0.005**	**0.0002**	**0.0001**

* (8,13,15,16)
† (2,13,16)
Note: Single and multiple, exercise-enhanced prebreathe studies were combined to allow comparison of exercise-enhanced prebreathe with resting prebreathe controls.

It is also of note that the level of VGE and Gr4 VGE following EEP are neither higher nor occur earlier than in the resting prebreathe controls (Table IV; $P < 0.0002$). This result is not consistent with an earlier report by Conkin & Powell (3) which advocated adynamia as a DCS-protective measure. Although one of the EEP exposure conditions incorporated adynamic prebreathe and exposure (not walking during prebreathe or exposure) (2), the resulting 44% DCS incidence was not different from the 42% incidence

during dynamic exposure. Both experiments utilized EEP and nearly matched the 40% DCS incidence following a 4-h resting prebreathe (16).

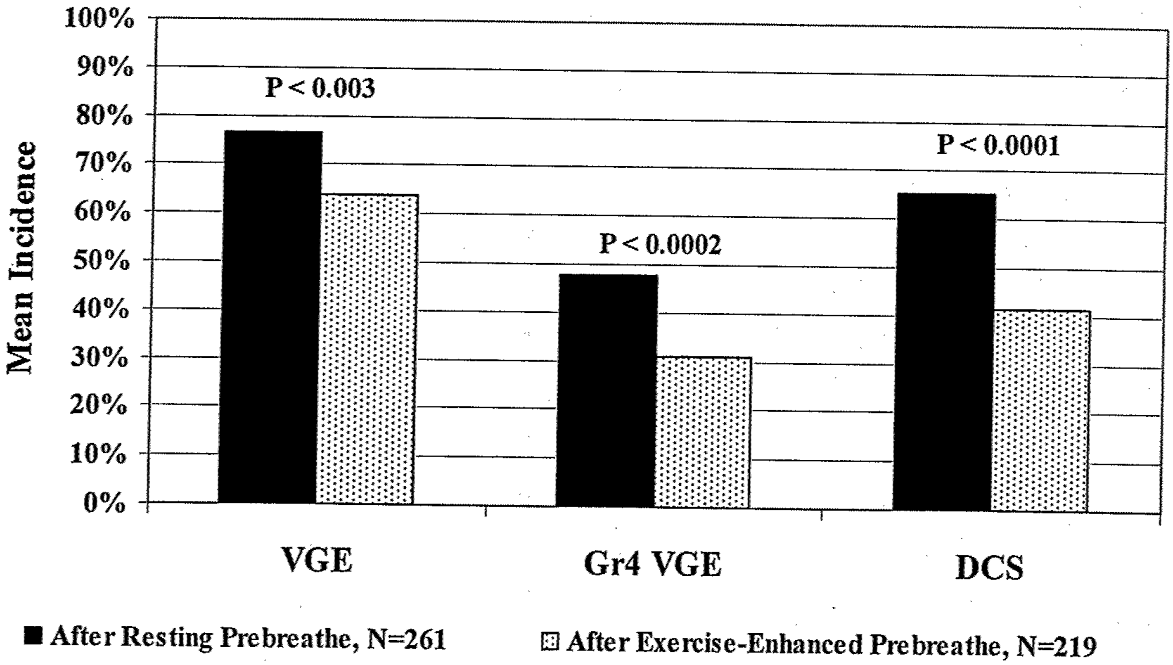

Fig. 2. DCS following resting and exercising prebreathe; 4-h exposures to 7620 m and 9144 m.

CONCLUSIONS

Multiple-exercise enhancement of prebreathe (MEEP) prior to 7620-m exposures provides similar protection from DCS as the longer, resting prebreathe procedures. A review of single-EEP and MEEP prior to high altitude exposures showed significantly less DCS than found after an equivalent period of resting prebreathe. Operational implementation of the procedure could shorten preflight procedures before long-duration exposures to 7620 m where lack of prebreathe has been shown to result in 80% DCS and serious symptoms.

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